REMARKS

Claims 1-35 are pending in the above-identified application and have been subjected to restriction by the aforesaid Restriction Requirement under 35 U.S.C. §121 and 37 C.F.R. §1.499 as follows:

Group 1, Claim(s) 1-19 (in part), drawn to Formula I compounds in which Y is an Asp derivative, X is hydrogen; and first method of use in treating stroke.

Group 2, Claim(s) 1-19 (in part), drawn to Formula I compounds in which Y is an Asp derivative, X is an (un)substituted aryl group substituted aminosulfoxide (two structures on Page 94, lines 15 and 20); and first method of use in treating stroke.

Group 3, Claim(s) 1-19(in part), drawn to Formula I compounds in which Y is an Asp derivative, X is dimethyl cyclohexyl(one) substituted aminosulfoxide (3 structures on pages 94-95); and first method of use in treating stroke.

Group 4, Claim(s) 1-19(in part), drawn to Formula I compounds in which Y is an Asp derivative, X is dimethylcyclopentanone substituted aminosulfoxide (second structure on page 95); and first method of use in treating stroke.

Group 5, Claim(s) 1-19 (in part), drawn to Formula I compounds in which Y is an Asp derivative, X is an (un)substituted aryl group substituted alkylsulfinyl (fourth and fifth structures on Page 95); and first method of use in treating stroke.

Group 6, Claim(s) 1-19 (in part), drawn to Formula I compounds in which Y is an Asp derivative, X is the fifth structure on Page 95; and first method of use in treating stroke.

Group 7, Claim(s) 1-19 (in part), drawn to Formula I compounds in which Y is an Asp derivative, X is the sixth structure on Page 95; and first method of use in treating stroke.

Group 8, Claim(s) 1-5 (in part) and 8-19 (in part), drawn to Formula I compounds in which Y is a succinimyl derivative (second Y structure on page 93) and first method of use in treating stroke.

Group 9, Claim(s) 1-5 (in part) and 8-19 (in part), drawn to Formula I compounds in which Y is a cyano derivative (third structure on page 93); and first method of use in treating stroke.

Groups 10-18, Claim(s) 20-23, drawn to second method of using a compound of one of Groups 1 to 9 above to treat inflammation.

Groups 19-27, Claim(s) 24-25, drawn to third method of using a compound of one of Groups 1 to 9 above to treat septic shock.

Groups 28-36, Claim(s) 26-27, drawn to fourth method of using a compound of one of Groups 1-9 above to treat reperfusion injury.

Groups 37-45, Claim(s) 28-29, drawn to fifth method of using a compound of one of Groups 1-9 above to treat Alzheimer's.

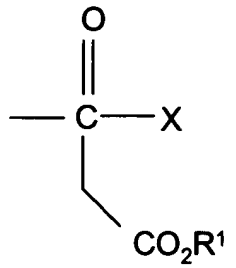
Groups 46-54, Claim(s) 30-31, drawn to sixth method of using a compound of one of Groups 1-9 above to treat shigelolosis.

Groups 55-63, Claim(s) 32-33, drawn to seventh method of using a compound of one of Groups 1-9 above to treat multiple sclerosis.

Groups 64-72, Claim(s) 34-35, drawn to eighth method of using a compound of one of Groups 1-9 above to inhibit ICE.

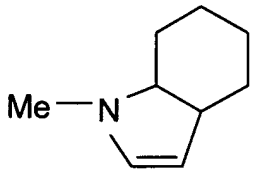
In support of the Restriction Requirement, the Office Action alleges that the inventions listed as Groups do not relate to a single general inventive concept under PCT Rule 13.1 because the compounds lack the same or corresponding special technical features. More specifically, according to the Office Action, the Group 1-9 compounds lack a significant structural element (e.g., core) which is shared by all of the alternatives which elicits a common activity and that the different alternatives do not represent a recognized class of chemical compounds so as to constitute a proper Markush group. See, Office Action, page 4. Further, the Office Action alleges that the alleged lack of significant structure shared by Groups 1-9 preclude the ability to conduct a meaningful search. The Office Action further alleges that Groups 10-72 represent further methods of use which represent different and diverse diseases or condition which require different etiologies and fail to share a special technical feature.

As indicated hereinabove, and in order to be responsive to the Restriction Requirement, applicants provisionally elect, with traverse, the subject matter of Group III, Claims 1-19 (in part), drawn to compounds of Formula I, in which Y is an Asp derivative, X is dimethyl cyclohexyl(one) substituted aminosulfoxide and first method of use in treating stroke. Further, in order to be responsive to the specification applicants elect the species, with traverse, of Example 31, the structure of which is depicted on Page 63 of the specification, i.e., where

Y is 

R is H;

X is the fourth element in its definition; n is 1, R^1 is H; R^4 is isopropyl, R^3 is H, and R^2 is $(CH_2)_2$- substituted heteroaryl, wherein the substituent is methyl, i.e., in this case, R^2 is



Nevertheless, applicants reserve the right to file one or more divisional application(s) directed to the non-elected subject matter.

Notwithstanding the foregoing, applicants hereby traverse, pursuant to 37 C.F.R. §§1.111 and 1.143, the requirement for a restriction and request reconsideration thereof in view of the following remarks.

Applicants respectfully request that the Restriction Requirement be withdrawn since it is not in compliance with 35 U.S.C. §121 and 37 C.F.R. §§1.141 and 1.142 and 1.499. 35 U.S.C. §121 provides that the Commissioner may restrict an application when two or more independent and distinct inventions are claimed in a single application (emphasis added). Similarly, 37 C.F.R. §1.141(a) permits restriction on condition that independent and distinct inventions are found within one application.

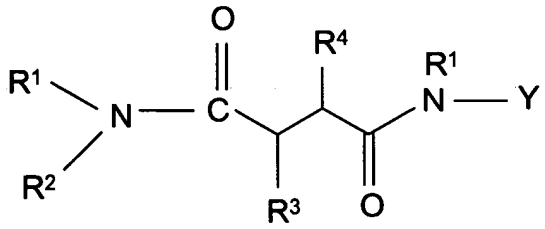
There is absolutely no indication in the Office Action that Groups 1-72 are also independent. In fact, applicants submit that there is an interdependence between each of the groups alleged to be patentably distinct.

MPEP §802.01 defines independent as follows:

> The term "independent" (i.e., not dependent) means that there is no disclosed relationship between the two or more subjects disclosed, that is they are unconnected in design, operation or effect...

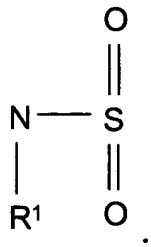
Applicants respectfully submit that the subject matter in Groups 1-72 are connected in design, operation or effect and are thus not dependent.

The subject matter of Groups 1-72 relate to compounds having the formula



In all of the groups, whether composition of matter or process claims, the compounds can be depicted by the above-core structure. Moreover, the Y substituents, are not as diverse as the Office Action has alleged since all of them have a common functionality, i.e., they are either an acid or ester. For example, when R´ is H, the first and third structures are acids and when R is alkyl, they are esters; while the second structure is an internal ester (or lactone). Further, contrary to the allegations in the Office Action, the various X groups are not as diverse as alleged by the Office Action. For example, the second –seventh

structures of X only differ by the identity of the cyclic structure at the end of the molecule. Moreover, the eighth and ninth structures in the definition of X differs slightly from the second and third definitions of X in that the only difference is an S-group substituted for an



Moreover, the last two structures of X also belong in the second group of X as they are directed to a homolog-like molecule in which the $(CH_2)_n$-O group substitutes for (CH_2) S or $(CH_2)_n$-(R_1)N-$S(O)_2$-group, respectively and the groups to which the O is attached is an heteroaryl group, rather than aryl group.

Thus, there are various features in common on the Y substituents. Further, the X substitutents in the aspartyl-like moiety have several features in common. Thus, contrary to the allegations in the Office Action, the structures of Formula I have a significant core structure shared by Groups 1-9. Moreover, since all of the compounds in the composition of matter claims and the use claims share this common structure, there is unity of invention.

Thus, Groups 1-72 are related and are not independent. They therefore have a disclosed relationship. Consequently, because these groups of claims are connected in design, operation and/or effect and are therefore not independent, the claims which the Office Action has grouped separately are not "independent and distinct" so as to justify the Restriction

Requirement. It is therefore respectfully submitted that the Restriction Requirement is improper and cannot be maintained.

Moreover, since the subject matter of these 72 groups are linked to form a single general inventive concept for the reasons given hereinabove, a restriction requirement in this case is improper. This application is claiming priority of an international application, and as such, pursuant to 37 C.F.R. §1.499, the Examiner cannot issue a restriction requirement if the claimed subject matter has unity of the invention. In the present case, there is unity of invention between Groups 1-72. Consequently, inasmuch as there is a unity of invention, it is respectfully requested that the restriction requirement be withdrawn.

In addition, the courts have recognized that it is in the public interest to permit applicants to claim several aspects of their invention together in one application, as the applicants have done herein, so as to encourage applicants to provide a more detailed disclosure of all aspects of their invention. The CCPA has observed:

> We believe the constitutional purpose of the patent system is promoted by encouraging applicants to claim, and therefore to describe in the manner recognized by 35 U.S.C. §112, all aspects as to what they regard as their invention, regardless of the number of statuory classes involved.

In re Kuehl, 456 F2d 658, 666, 117 U.S.P.Q. 250, 256 (CCPA 1973).

Applicants respectfully suggest that in view of the continued increase of official fees and the potential limitation of applicants' financial resources, a practice which arbitrarily imposes a Restriction Requirement may become prohibitive and thereby

contravenes the constitutional intent to promote and encourage the progress of science and the useful arts. Moreover, under the regulatory changes as a consequence of the General Agreement on Trade and Tariffs (GATT), the applicants are required to either conduct simultaneous prosecution with attendant filing fees and costs or face a compromise of the term of their patent assets. This is especially true in the present case wherein the Office Action has imposed a burdensome restriction requirement, requiring applicants to file 72 cases in order to have the claimed subject matter to be examined in its entirety.

It is vital to all applicants that Restriction Requirements issue only with the proper statutory authorization, because patents issuing on divisional applications which are filed to prosecute claims that the Examiner held to be independent and distinct can be vulnerable to legal challenges alleging double-patenting. The third sentence of U.S.C. §121, which states that a patent issuing on a parent application "shall not be used as a reference" against a divisional application or a patent issued thereon, does not provide comfort against such allegations. The Court of Appeals for the Federal Circuit has declined to hold that §121 protects a patentee from an allegation of same-invention-double-patenting, Studiengesellschaft Kohle mbH v. Northern Petrochemical Co., 784 F.2d 351, 355, 288 U.S.P.Q. 837, 840 (Fed. Cir. 1986); and in Gerber Garment Technology Inc. v. Lectra Systems Inc., 916 F.2d 683, 16 U.S.P.Q. 2d 1436 (Fed. Cir. 1990), that court held that §121 does not insulate a patentee from an allegation of "obviousness-type" double patenting, and in fact affirmed the invalidation on double patenting grounds of a patent that had issued from a divisional application filed following a restriction requirement. Furthermore, it is far from

clear that the step of filing a terminal disclaimer is available to resolve a double patenting issue that arises after the issuance of a patent on the divisional application.

All these considerations indicate that the imposition of a restriction requirement with inadequate authority can lead to situations in which applicant's legitimate patent rights are exposed to uncertainty and even extinguished. Accordingly, to protect patentee's rights and to serve the public's interest in the legitimacy of issued patents, applicant respectfully urges the Examiner not to require restriction in cases such as the present application.

The Office Action seems to justify the restriction requirement on the basis of the difficulty of the search. This of course is in error for several reasons.

The classification system is an unreliable basis for requiring restriction between claims to the various aspects of applicants' unitary invention, because the system exhibits considerable overlap in technical definitions. In particular, the definitions of subclasses in the classification system do not prevent an Examiner from basing patentability decisions, as to claims he assigned to one group, on patent references found in the subclass(es) with which he associated another group of claims.

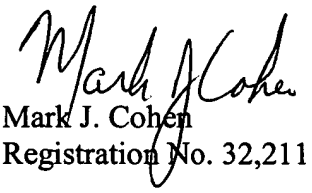
Furthermore, the classification system is a poor basis for requiring restriction between related aspects of an invention because classifications and definitions change over time. Thus, a classification that might have seemed to support restriction at a given time could change, thereby casting a shadow over the propriety of the restriction requirement later on during the term of the patents issuing from parent and divisional applications. Indeed,

classifications seem largely to change in response to considerations of administrative convenience, and often in response to nothing more than growth in the number of patents in a given class or subclass. These considerations have nothing to do with whether the subject matter of patents assigned to different classifications is "independent and distinct" as those terms are used in 35 U.S.C. §121, which fact proves that basing restriction requirements on the classification system is improper.

Hence, it is respectfully requested that the United States Patent and Trademark Office reconsider and withdraw the requirement for restriction pursuant to 35 U.S.C. §121 and provide an action on the merits with respect to all of the claimed subject matter.

Applicants welcome discussions with the Examiner to discuss the Restriction Requirement and the applicants' response thereto.

Respectfully submitted,



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